

Hines 09/746,581 < page>

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FILE COVERS 1907 - 9 Apr 2002 VOL 136 ISS 15
FILE LAST UPDATED: 8 Apr 2002 (20020408/ED)

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=> d stat que
L1 6 SEA FILE=HCAPLUS ("MOSTE C"/AU OR "MOSTE CATHERINE"/AU OR
"MOSTE CATHERINE"/IN OR "MOSTE DESHAIRS CATHERINE"/AU OR
"MOSTE DESHAIRS CATHERINE"/IN)
L2 27 SEA FILE=HCAPLUS ("MEIGNIER B"/AU OR "MEIGNIER BERNARD"/AU OR
"MEIGNIER BERNARD"/IN)
L3 28 SEA FILE=HCAPLUS L1 OR L2

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L3 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:520224 HCAPLUS
DOCUMENT NUMBER: 136:230831
TITLE: Modulation of the antibody response to the HIV
envelope subunit by co-administration of infectious or
heat-inactivated canarypoxvirus (ALVAC) preparations
AUTHOR(S): Boudet, F.; Chevalier, M.; Jourdier, T. M.; Tartaglia,
J.; **Moste, C.**

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CORPORATE SOURCE: Campus Merieux, Aventis Pasteur, Marcy l'Etoile,
69280, Fr.

SOURCE: Vaccine (2001), 19(30), 4267-4275
CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Poxviruses are large DNA viruses capable of infecting a broad range of animal species. Infection is generally accompanied by an inflammatory response in the host, the extent of which varies considerably with the specific poxvirus and host species. Regarding ALVAC, a poxvirus derived from the canarypox vaccine strain, Kanapox, and which represents a promising immunization vehicle in humans, nothing is known about its inflammatory capacity. The present study was aimed at documenting this issue in rodents, including mice and guinea pigs. It was then attempted to evaluate how such properties could influence the immunogenicity of an antigen concomitantly administered with ALVAC preps. using the HIV envelope subunit, rgp160, as the model immunogen. The results revealed that ALVAC, either infectious or heat-inactivated, induced in both animal species an early inflammatory response, as evidenced by a rapid migration of neutrophils to the site of inoculation. In parallel, the canarypoxvirus was shown to strongly adjuvant the co-administered immunogen, resulting in a marked increase in Env-specific IgG, IgG1 and particularly IgG2(a) serum titers. Of further interest, the heat-inactivated prepn. of ALVAC retained this immunostimulatory activity. Whether or not a link between the inflammatory and immunomodulatory properties of ALVAC exists remains to be established, but such features are clearly interesting with respect to the potential use of ALVAC as an immunization vehicle.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:15035 HCPLUS

DOCUMENT NUMBER: 132:69299

TITLE: Mucosal targeting immunization comprising immunogens

INVENTOR(S): Jourdier, Therese; Moste, Catherine;

Meignier, Bernard

PATENT ASSIGNEE(S): Pasteur Merieux Serums & Vaccins, Fr.

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|---|----------|-----------------|----------|
| WO 2000000218 | A1 | 20000106 | WO 1999-FR1554 | 19990628 |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, | | | |

MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 9943761 A1 20000117 AU 1999-43761 19990628
 EP 1087788 A1 20010404 EP 1999-926558 19990628
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
 US 2001021384 A1 20010913 US 2000-746581 20001221
 PRIORITY APPLN. INFO.: FR 1998-8354 A 19980626
 WO 1999-FR1554 W 19990628

AB The invention concerns the use of an immunogen specific of a pathogenic agent with a gateway in the buccal mucous membrane region, for producing a vaccine compn. to be administered in the floor of the mouth in a human being so as to develop directly a local response in IgA antibodies and in B cells secreting IgA in the buccal mucous membrane, saliva and ganglions draining said mucous membrane. The invention also concerns a vaccine compn. capable of being applied in the floor of the mouth in a human being to induce local and systemic immunity in IgA antibodies, substantially consisting of a material adhering or not to the buccal mucous membrane and contg. an immunogen specific of the pathogenic agent with a gateway into the buccal mucous membrane. Capsules contg. starch and hydroxyapatite particles comprising lyophilized antigens of cytomegalovirus or hepatitis A were prep'd. The capsules were slowly dissolved inside the mouth. The hydroxyapatite facilitated the penetration of the immunogens through the mucosa.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:15033 HCPLUS
 DOCUMENT NUMBER: 132:69298
 TITLE: Mucosal targeting immunization comprising immunogens
 INVENTOR(S): Jourdier, Therese; Moste, Catherine;
 Meignier, Bernard
 PATENT ASSIGNEE(S): Pasteur Merieux Serums & Vaccins, Fr.
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2000000217 | A1 | 20000106 | WO 1999-FR1539 | 19990625 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |

AU 9943754 A1 20000117 AU 1999-43754 19990625
 EP 1089758 A1 20010411 EP 1999-926545 19990625
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
 PRIORITY APPLN. INFO.: FR 1998-8353 A 19980626
 WO 1999-FR1539 W 19990625

AB The invention concerns the use of an immunogen specific of a pathogenic agent having a gateway in a mucous membrane for producing an immunogenic compn. to be administered to a human by parenteral route at the surface of part of the body distinct from the mucous membrane so as to directly develop a local response in IgA, IgG and/or IgM antibody in said mucous membrane. Vaccines against Herpes simplex, Candida, Chlamydia, human Papilloma virus, genital Mycoplasma, and Treponema pallidum was prepd. and injected to the buttocks muscle to stimulate local IgA antibody response in rectal, genital and urinary mucosa.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:15031 HCAPLUS
 DOCUMENT NUMBER: 132:77612
 TITLE: Use of poxviruses as enhancer of specific immunity
 INVENTOR(S): Chevalier, Michel; Meignier, Bernard;
 Moste, Catherine; Sambhara, Suryaprakash
 PATENT ASSIGNEE(S): Pasteur Merieux Serums et Vaccins, Fr.
 SOURCE: PCT Int. Appl., 63 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2000000216 | A2 | 20000106 | WO 1999-EP4913 | 19990628 |
| WO 2000000216 | A3 | 20000316 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9950368 | A1 | 20000117 | AU 1999-50368 | 19990628 |
| EP 1087789 | A2 | 20010404 | EP 1999-934677 | 19990628 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| PRIORITY APPLN. INFO.: | | | EP 1998-420110 | A 19980626 |
| | | | EP 1998-420111 | A 19980626 |
| | | | WO 1999-EP4913 | W 19990628 |

AB The invention relates to a method for enhancing the specific immune response against an immunogenic compd. which comprises administering the immunogenic compd. together with a poxvirus recombinant and a vaccinal antigen, which is not a poxvirus. The immunol. material may be any biol.

material useful as a vaccine e.g. , a polypeptide characteristic of a pathogenic microorganism or assocd. with a tumoral disorder, a DNA plasmid encoding a peptide or a polypeptide characteristic of a pathogenic microorganism or a tumor-assocd. antigen, or an hapten coupled to a carrier mol. The poxvirus may be a live, attenuated or inactivated virus or a recombinant virus. Recombinant virus may encode a heterologous polypeptide such as chemokines, cytokines or co-immunostimulatory mols. or an homologous polypeptide, which is immunol. cross reactive with the immunogenic polypeptide or peptide.

L3 ANSWER 5 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:314834 HCPLUS
DOCUMENT NUMBER: 131:143198
TITLE: Safety and immunogenicity of a live recombinant canarypox virus expressing HIV type 1 gp120 MN tm/gag/protease LAI (ALVAC-HIV, vCP205) followed by a p24E-V3 MN synthetic peptide (CLTB-36) administered in healthy volunteers at low risk for HIV infection
AUTHOR(S): Salmon-Ceron, Dominique; Excler, Jean-Louis; Finkielsteyn, Laurent; Autran, Brigitte; Gluckman, Jean-Claude; Sicard, Didier; Matthews, Thomas J.; Meignier, Bernard; Valentin, Christian; El Habib, Raphaelle; Blondeau, Christine; Raux, Maurice; Moog, Christiane; Tartaglia, James; Chong, Pele; Klein, Michel; Milcamps, Bruno; Heshmati, Farad; Plotkin, Stanley
CORPORATE SOURCE: The Agis Group, CHU Cochin AP HP, Universite Paris 5, Paris, 75679, Fr.; L'Agence Nationale De Recherches Sur Le Sida
SOURCE: AIDS Res. Hum. Retroviruses (1999), 15(7), 633-645
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A live recombinant canarypox vector expressing HIV-1 gp120 MN tm/gag/protease LAI (ALVAC-HIV, vCP205) alone or boosted by a p24E-V3 MN synthetic peptide (CLTB-36) was tested in healthy volunteers at low risk for HIV infection for their safety and immunogenicity. Both antigens were well tolerated. ALVAC-HIV (vCP205) induced low levels of neutralizing antibodies against HIV-1 MN in 33% of the volunteers. None of them had detectable neutralizing antibodies against a nonsyncytium-inducing HIV-1 clade B primary isolate (Bx08). After the fourth injection of vCP205, CTL activity was detected in 33% of the volunteers and was directed against Env, Gag, and Pol. This activity was mediated by both CD4+ and CD8+ lymphocytes. On the other hand, the CLTB-36 peptide was poorly immunogenic and induced no neutralizing antibodies or CTLs. Although the ALVAC-HIV (vCP205) and CLTB-36 prime-boost regimen was not optimal, further studies with ALVAC-HIV (vCP205) are warranted because of its clear induction of a cellular immune response and utility as a priming agent for other subunit antigens such as envelope glycoproteins, pseudoparticles, or new peptides.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3 ANSWER 6 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:741948 HCPLUS
DOCUMENT NUMBER: 130:137886
TITLE: Canarypox virus-based vaccines: prime-boost strategies
to induce cell-mediated and humoral immunity against
HIV
AUTHOR(S): Tartaglia, James; Excler, Jean-Louis; El Habib,
Raphaelle; Limbach, Keith; **Meignier, Bernard**
; Plotkin, Stanley; Klein, Michel
CORPORATE SOURCE: Virogenetics Corporation, Troy, NY, 12180, USA
SOURCE: AIDS Res. Hum. Retroviruses (1998), 14(Suppl. 3),
S291-S298
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 58 refs. discussing clin. evaluation of prime-boost regimens
utilizing ALVAC-based recombinants.
REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:667640 HCPLUS
DOCUMENT NUMBER: 130:79901
TITLE: Potential improvements for poxvirus-based immunization
vehicles
AUTHOR(S): Tartaglia, James; Benson, John; Cornet, Bernard; Cox,
William I.; El Habib, Raphaelle; Excler, Jean-Louis;
Franchini, Genoveffa; Goebel, Scott; Jacobs, Bertram
L.; Klein, Michel; Limbach, Keith; Martinez, Hector;
Meignier, Bernard; Pincus, Steven; Plotkin,
Stanley
CORPORATE SOURCE: Virogenetics Corporation, Troy, NY, USA
SOURCE: Retroviruses Hum. AIDS Relat. Anim. Dis., Colloq. Cent
Gardes, 11th (1998), Meeting Date 1997, 187-197.
Editor(s): Girard, Marc; Dodet, Betty. Elsevier:
Paris, Fr.
CODEN: 66UXAF
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 22 refs. The author discusses the use of poxviruses as
vectors for vaccines, modulation of eIF-2.alpha. phosphorylation state,
modulation of poxvirus early transcription factors, and expression of
cytokines as immunoadjuvants.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:571106 HCPLUS
DOCUMENT NUMBER: 129:314713
TITLE: Fine specificity of anti-V3 antibodies induced in
chimpanzees by HIV candidate vaccines
Coeffier, Eliane; Girard, Marc; Barre-Sinoussi,
Francoise; **Meignier, Bernard**; Muchmore,

CORPORATE SOURCE: Elizabeth; Fultz, Patricia N.; LeClerc, Claude
Unite de Biologie des Regulations Immunitaires,
Institut Pasteur, Paris, 75015, Fr.
SOURCE: AIDS Res. Hum. Retroviruses (1998), 14(12), 1023-1034
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The fine specificity of the anti-V3 antibody responses induced in chimpanzees immunized by various human immunodeficiency type 1 (HIV-1) candidate vaccines and challenged by heterologous strains of HIV-1 was analyzed by ELISA and Pepscan epitope mapping. Two chimpanzees immunized with the recombinant canarypox virus ALVAC-HIV (vCP125) expressing gp160MN and boosted with purified gp160MN/LAI alone, then with both immunogens in combination, were not protected against challenge with HIV-1 SF2. Their sera mainly recognized one epitope of the V3 loop, located in the N-terminal half. By contrast, immunization of two other chimpanzees with purified gp160MN/LAI and boosting with a synthetic V3MN peptide elicited a strong anti-V3 antibody response with a broader specificity directed against multiple epitopes all along the V3 loop. These chimpanzees were protected against infection by HIV-1 SF2. However, when these two chimpanzees were challenged later with a HIV-1 clade E strain virus, they became infected. The authors failed to detect any reactivity with the peptide of the ectodomain of gp41 of sera harvested after immunization with the various immunogens or after challenge with HIV-1 SF2 or HIV-1 90CR402. These results demonstrated that anti-V3 antibodies with a restricted fine specificity were induced in chimpanzees immunized with gp160 purified or expressed by recombinant canarypox confirming the authors' previous results obtained in three different species (human, guinea pig and, macaque). In contrast, a boost with the V3 peptide broadened antibody responses, suggesting that the mode of presentation of the V3 loop to the immune system strongly influences the epitope specificity of the resulting antibody response.

L3 ANSWER 9 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:792277 HCPLUS
DOCUMENT NUMBER: 128:60492
TITLE: Restricted specificity of anti-V3 antibodies induced
in humans by HIV candidate vaccines
AUTHOR(S): Coeffier, Eliane; Excler, Jean-Louis; Kieny, Marie
Paule; Meignier, Bernard; Moste,
Catherine; Tartaglia, James; Pialoux, Gilles;
Salmon-Ceron, Dominique; Leclerc, Claude
CORPORATE SOURCE: Unite de Biologie des Regulations Immunitaires,
Institut Pasteur, Paris, 75015, Fr.
SOURCE: AIDS Res. Hum. Retroviruses (1997), 13(17), 1471-1485
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors analyzed the fine specificity of anti-V3 antibodies elicited in 3 different species (human, guinea pig, and macaque) by various HIV candidate vaccines. Following immunization with recombinant canarypox virus expressing gp160MN or with recombinant gp160MN/LAI, this antibody

response was shown to be directed against the N-terminal region of the V3 loop. Although this response was increased by a prime-boost regimen using immunization with canarypox expressing gp160 followed by an rgp160 boost, its specificity remained restricted mainly to the recognition of this region of the V3 loop. Pepscan anal. of sera confirmed the results obtained by ELISA and allowed the definition of an immunodominant common binding site for these sera located within the sequence NKRKRIHIGPGR. In contrast to these results, a boost with the V3 peptide was shown to broaden the antibody response and pepscan anal. showed that sera from individuals boosted with the V3 synthetic peptide recognize determinants all along the V3 loop. Similar fine specificity of anti-V3 antibodies was obtained in human, guinea pig, and macaque following immunization by a prime-boost regimen using canarypox recombinants expressing gp160 or gp120 and purified rgp160. In contrast, a V3 synthetic peptide boost stimulated the prodn. of antibodies that recognize multiple epitopes within the V3 loop. Because the induction of antibodies that recognize multiple sites in the V3 loop could be of major importance to neutralize different HIV isolates, these results may have implications for the design and selection of HIV candidate vaccines.

L3 ANSWER 10 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:630626 HCPLUS

DOCUMENT NUMBER: 125:273107

TITLE: Failure of a human immunodeficiency virus type 1 (HIV-1) subtype B-derived vaccine to prevent infection of chimpanzees by an HIV-1 subtype E strain

AUTHOR(S): Girard, Marc; Yue, Ling; Barre-Sinoussi, Francoise; van der Ryst, Elna; Meignier, Bernard; Muchmore, Elizabeth; Fultz, Patricia N.

CORPORATE SOURCE: Inst. Pasteur, Paris, 75015, Fr.

SOURCE: J. Virol. (1996), 70(11), 8229-8233

CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Generation of an effective vaccine against human immunodeficiency virus type 1 (HIV-1) must overcome problems assocd. with extensive genetic diversity. Although we previously reported vaccine-induced protection of chimpanzees against infection with an HIV-1 strain different from the one used to make the immunogens, both the HIV-1 vaccine and challenge strains were classified within subtype B. To det. whether the HIV-1-specific immunity elicited might also prevent infection by a strain of HIV-1 from a different clade, the same chimpanzees were given booster inoculations with the rgp160-MN/LAI (recombinant hybrid gp160 mol.) and V3-MN immunogens and then were challenged by i.v. inoculation of a comparable dose of a subtype E HIV-1 from the Central African Republic. Both animals became infected with the subtype E virus, indicating that intraclade vaccine-mediated protection does not predict interclade protection, at least in the context of i.v. challenge and the HIV-1 strains used. This study has important implications for planned phase III efficacy trials of similar vaccine preps. in Thailand where HIV-1 subtype B and E strains cocirculate.

L3 ANSWER 11 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:438751 HCPLUS

DOCUMENT NUMBER: 125:84076

TITLE: Human safety and immunogenicity of a canarypox-rabies glycoprotein recombinant vaccine: An alternative poxvirus vector system

AUTHOR(S): Fries, L. F.; Tartaglia, J.; Taylor, J.; Kauffman, E. K.; Meignier, B.; Paoletti, E.; Plotkin, S.

CORPORATE SOURCE: School Hygiene and Public Health, Johns Hopkins University, Baltimore, MD, 21205, USA

SOURCE: Vaccine (1996), 14(5), 428-434

CODEN: VACCDE; ISSN: 0264-410X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Avian poxvirus recombinants undergo abortive replication in nonavian cells, yet can achieve expression of extrinsic gene products. Canarypox-vectored vaccines have been innocuous and immunogenic in several mammalian species. ALVAC-RG, a canarypox recombinant expressing the rabies glycoprotein gene, was inoculated i.m. into adult volunteers on days 0, 28, and 180. Sequential cohorts received 103.5, 104.5, and 105.5 TCID50; addnl. volunteers received the std. human diploid cell rabies vaccine (HDCV) on the same schedule. Reactogenicity of ALVAC-RG was minimal. The lowest dose of ALVAC-RG induced little antibody to rabies virus by ELISA or rapid fluorescent focus inhibition test (RFFIT), but 104.5 and 105.5 TCID50 doses elicited responses in both assays. All recipients of 104.5 and 105.5 TCID50 of ALVAC-RG attained RFFIT values above the presumed protective level. Canarypox-specific immune responses did not inhibit boosting of rabies-specific antibodies by the day 180 dose of ALVAC-RG. T cell proliferation in response to inactivated rabies virus in vitro was similar in HDCV and ALVAC-RG recipients after the first and second doses, although HDCV yielded superior results after the third dose. ALVAC-RG was safe in humans, induced functional antibody to rabies glycoprotein, elicited cellular responses to rabies virus, and could be used successfully for booster dosing at a 6 mo interval.

L3 ANSWER 12 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:433157 HCPLUS

DOCUMENT NUMBER: 125:139436

TITLE: African green monkey kidney (Vero) cells provide an alternative host cell system for influenza A and B viruses

AUTHOR(S): Govorkova, E. A.; Murti, G.; Meignier, B.; de Taisne, C.; Webster, R. G.

CORPORATE SOURCE: Department Virology & Molecular Biology, St. Jude Children's Hospital, Memphis, TN, 38105, USA

SOURCE: J. Virol. (1996), 70(8), 5519-5524

CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The prepn. of live, attenuated human influenza virus vaccines and of large quantities of inactivated vaccines after the emergence or reemergence of a pandemic influenza virus will require an alternative host cell system, because embryonated chicken eggs will likely be insufficient and suboptimal. Preliminary studies indicated that an African green monkey kidney cell line (Vero) is a suitable system for the primary isolation and cultivation of influenza A viruses. The authors now demonstrate for the first time that Vero cells are suitable for the isolation and productive

replication of influenza B viruses and det. the biol. and genetic properties of both influenza A and B viruses in Vero cells; addnl., the authors characterize the receptors on Vero cells compared with those on Madin-Darby canine kidney (MDCK) cells. Sequence anal. indicated that the hemagglutinin of Vero cell-derived influenza B viruses was identical to that of MDCK-grown counterparts but differed from that of egg-grown viruses at amino acid positions 196 to 198. Fluorescence-activated cell sorting anal. showed that although Vero cells possess predominantly α .2,3 galactose-linked sialic acid, they are fully susceptible to infection with either human influenza A or B viruses. Moreover, all virus-specific polypeptides were synthesized in the same proportions in Vero cells as in MDCK cells. Electron microscopic and immunofluorescence studies confirmed that infected Vero cells undergo the same morphol. changes as do other polarized epithelial cells. Taken together, these results indicate that Vero cell lines could serve as an alternative host system for the cultivation of influenza A and B viruses, providing adequate quantities of either virus to meet the vaccine requirements imposed by an emerging pandemic.

L3 ANSWER 13 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:108140 HCPLUS

DOCUMENT NUMBER: 124:172869

TITLE: Safety and immunogenicity of a recombinant HIV type 1 glycoprotein 160 boosted by a V3 synthetic peptide in HIV-negative volunteers

AUTHOR(S): Salmon-Ceron, Dominique; Excler, Jean-Louis; Sicard, Didier; Blanche, Philippe; Finkielstzjen, Laurent; Gluckman, Jean-Claude; Autran, Brigitte; Matthews, Thomas J.; Meignier, Bernard; et al.

CORPORATE SOURCE: Hopital Cochin, Paris, Fr.

SOURCE: AIDS Res. Hum. Retroviruses (1995), 11(12), 1479-86

CODEN: ARHRE7; ISSN: 0889-2229

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The safety and the immunogenicity of a recombinant hybrid envelope glycoprotein MN/LAI (rgp 160) followed by booster injections of a V3 (MN) linear peptide were evaluated in HIV-neg. adults at low risk for HIV infection. Volunteers received either rgp160 in alum at 0, 1, and 6 mo (group A), rgp160 at 0 and 1 mo followed by V3 at 3 and 6 mo formulated in alum (group B), or in Freund's incomplete adjuvant (FIA) (group C). Local and systemic reactions were mild to moderate and resolved within the first 72 h after immunization. No significant biol. changes (routine tests and autoantibodies) were obsd. One month after the last injection in either group, neutralizing antibodies (NAs) against the HIV-1 MN isolate were detected in 4 of 5 (A), 7 of 10 (B), and 10 of 10 (C) subjects with significantly higher geometric mean titers in the latter group. Four of nine sera with the highest NA titers against MN weakly cross-neutralized the HIV-1 SF2 isolate; none had NA against the HIV-1 LAI strain or against a North American primary isolate. Specific lymphocyte T cell proliferation to rgp160 was detected in 92% of the subjects after the second injection of rgp160 and in 80% of them 12 mo after the first injection. A weak and short-lived envelope-specific CD4+ - mediated cytotoxic lymphocyte activity was detected at certain time points in few subjects. This prime-boost vaccine approach using rgp160 followed by a V3

peptide was safe in humans, and was able to elicit high levels of neutralizing antibodies and a strong and persistent T cell lymphoproliferative response to rgp160 and to V3. However, the neutralization response was restricted to the homologous HIV-1 strain and little env-specific cytotoxic activity was induced.

L3 ANSWER 14 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:812565 HCPLUS
DOCUMENT NUMBER: 123:225389
TITLE: Vaccine-induced protection of chimpanzees against infection by a heterologous human immunodeficiency virus type 1
AUTHOR(S): Girard, Marc; Meignier, Bernard;
Barre-Sinoussi, Francoise; Kieny, Marie-Paule;
Matthews, Thomas; Muchmore, Elizabeth; Nara, Peter L.;
Wei, Qing; Rimsky, Laurence; et al.
CORPORATE SOURCE: Inst. Pasteur, Paris, 75015, Fr.
SOURCE: J. Virol. (1995), 69(10), 6239-48
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The extraordinary genetic diversity of human immunodeficiency virus type 1 (HIV-1) is a major problem to overcome in the development of an effective vaccine. In the most reliable animal model of HIV-1 infection, chimpanzees were immunized with various combinations of HIV-1 antigens, which were derived primarily from the surface glycoprotein, gp160, of HIV-1 strains LAI and MN. The immunogens also included a live recombinant canarypox virus expressing a gp160-MN protein. In one expt., two chimpanzees were immunized multiple times; one animal received antigens derived only from HIV-1LAI, and the second animal received antigens from both HIV-1LAI and HIV-1MN. In another expt., four chimpanzees were immunized in parallel a total of five times over 18 mo; two animals received purified gp160 and V3-MN peptides, whereas the other two animals received the recombinant canarypox virus and gp160. At 3 mo after the final booster, all immunized and naive control chimpanzees were challenged by i.v. inoculation of HIV-1SF2; therefore, the study represented an intrasubtype B heterologous virus challenge. Virol. and serol. follow-up showed that the controls and the two chimpanzees immunized with the live recombinant canarypox virus became infected, whereas the other animals that were immunized with gp160 and V3-MN peptides were protected from infection. Evaluation of both cellular and humoral HIV-specific immune responses at the time of infectious HIV-1 challenge identified the following as possible correlates of protection: antibody titers to the V3 loop of MN and neutralizing antibody titers to HIV-1MN or HIV-1LAI, but not to HIV-1SF2. The results of this study indicate that vaccine-mediated protection against i.v. infection with heterologous HIV-1 strains of the same subtype is possible with some immunogens.

L3 ANSWER 15 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:445143 HCPLUS
DOCUMENT NUMBER: 119:45143
TITLE: NYVAC: A highly attenuated strain of vaccinia virus
AUTHOR(S): Tartaglia, James; Perkus, Marion E.; Taylor, Jill;
Norton, Elizabeth K.; Audonnet, Jean Christophe; Cox,

William I.; Davis, Stephen W.; Van der Hoeven,
Johanna; **Meignier, Bernard**; et al.
CORPORATE SOURCE: Virogenet. Corp., Troy, NY, 12180, USA
SOURCE: Virology (1992), 188(1), 217-32
CODEN: VIRLAX; ISSN: 0042-6822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A highly attenuated vaccinia virus strain, NYVAC (vP866), was derived from a plaque-cloned isolate of the Copenhagen vaccine strain by the precise deletion of 18 open reading frames (ORFs) from the viral genome. Among the ORFs deleted from NYVAC (vP866) are two genes involved in nucleotide metab., the thymidine kinase (ORFJ2R) and the large subunit of the ribonucleotide reductase (ORF 14L); the gene encoding the viral hemagglutinin (ORF A56R); the remnant (ORF A26L) of a highly expressed gene responsible for the formation of A-type inclusion bodies; the disrupted gene (ORFsB13R/B14R) normally encoding a serine protease inhibitor; and a block of 12 ORFs bounded by two known viral host range regulatory functions (ORFs C7L through K1L). Within this block, a secretory protein (ORF N1L) implicated in viral virulence and a functional complement 4b binding protein (ORF C3L) are encoded. The ORFs were deleted in a manner which prevents the synthesis of undesirable novel gene products. The attenuation characteristics of the derived NYVAC strain were compared in in vitro and in vivo studies with those of the Western Reserve (WR) lab. strain, the New York City Board of Health vaccine strain (Wyeth), the parental plaque-cloned isolate (VC-2) of the Copenhagen vaccine strain used to derive NYVAC, and the avipox virus canarypox (ALVAC), which is naturally restricted for replication to avian species. The NYVAC strain was demonstrated to be highly attenuated by the following criteria: (a) no detectable induration or ulceration at the site of inoculation on rabbit skin; (b) rapid clearance of infectious virus from the intradermal site of inoculation on rabbit skin; (c) absence of testicular inflammation in nude mice; (d) greatly reduced virulence, as demonstrated by the results of intracranial challenge of both 3-wk-old or newborn mice; (e) greatly reduced pathogenicity and failure to disseminate in immunodeficient (nude or cyclophosphamide treated) mice; and (f) dramatically reduced ability to replicate on a variety of human tissue culture cells. Despite these highly attenuated characteristics, the NYVAC strain, as a vector, retains the ability to induce strong immune responses to extrinsic antigens.
L3 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:590116 HCAPLUS
DOCUMENT NUMBER: 117:190116
TITLE: Influenza virus vaccine composition having a synergistic effect and containing influenza virus core as an additive
INVENTOR(S): **Moste-Deshairs, Catherine; Meignier, Bernard**
PATENT ASSIGNEE(S): Pasteur Merieux Serums et Vaccins, Fr.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9213002 | A1 | 19920806 | WO 1992-FR66 | 19920124 |
| W: AU, CA, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| FR 2671974 | A1 | 19920731 | FR 1991-806 | 19910124 |
| FR 2671974 | B1 | 19950303 | | |
| CA 2078985 | AA | 19920725 | CA 1992-2078985 | 19920124 |
| AU 9212487 | A1 | 19920827 | AU 1992-12487 | 19920124 |
| AU 654699 | B2 | 19941117 | | |
| ZA 9200510 | A | 19921125 | ZA 1992-510 | 19920124 |
| EP 522138 | A1 | 19930113 | EP 1992-904852 | 19920124 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE | | | | |
| IL 100765 | A1 | 19960618 | IL 1992-100765 | 19920124 |
| US 5741493 | A | 19980421 | US 1995-375224 | 19950119 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | FR 1991-806 | 19910124 |
| | | | WO 1992-FR66 | 19920124 |
| | | | US 1992-927261 | 19921122 |

AB An influenza vaccine is provided which is a std. influenza vaccine to which is added influenza virus core (or a fraction thereof), esp. a fraction contg. protein M. The added component improves the effectiveness of the vaccine. Purifn. of viral core from influenza virus NIB16 (A/H1N1) is described, as is prepn. of a core fraction contg. protein M. Addn. of the core material to the vaccine had a significant synergistic effect when the vaccine was tested in mice.

L3 ANSWER 17 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:446144 HCPLUS
 DOCUMENT NUMBER: 117:46144
 TITLE: Comparison of the ability of formalin-inactivated respiratory syncytial virus, immunopurified F, G and N proteins and cell lysate to enhance pulmonary changes in Balb/c mice
 AUTHOR(S): Vaux-Peretz, Fabienne; Chapsal, Jean Michel;
Meignier, Bernard
 CORPORATE SOURCE: Pasteur Mer. Serums Vaccins, Marcy l'Etoile, 69280, Fr.
 SOURCE: Vaccine (1992), 10(2), 113-18
 CODEN: VACCDE; ISSN: 0264-410X
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Formalin-inactivated respiratory syncytial virus (FI-RSV), a lysate of HEp-2 cells and proteins F, G and N, immunopurified from infected cell cultures, were compared for their ability to prevent injection and to enhance changes in lung cytol. assocd. with RSV challenge. Mice were immunized at 3 weekly intervals with serial dilns. of the preps. and challenged by the nasal route 1 wk after the last injection; their lungs were analyzed 4 days later. The concn. of the immunogens was adjusted to test at least a range of 2-500 ng of proteins per injection. The dose of FI-RSV used for immunization influenced both the protection against infection and the potentiation of lung histopathol. There was a strong correlation between the lesion scores and the proportion of larger cells recovered in bronchoalveolar lavage fluid. Cytol. changes were therefore

used as an index of lung alterations in further expts. Glycoproteins F and G, but not protein N, were protective against challenge infection. Potentiation was obsd. in mice immunized with minute amts. (2 ng per injection) of F, G, or N. HEp-2 cell lysate also caused potentiation but this required >125 ng of proteins per injection.

L3 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:18100 HCAPLUS
DOCUMENT NUMBER: 114:18100
TITLE: Genetic engineering and properties of novel herpes simplex viruses for use as potential vaccines and as vectors of foreign genes
AUTHOR(S): Meignier, Bernard; Roizman, Bernard
CORPORATE SOURCE: Inst. Merieux, Marcy L'Etoile, 69280, Fr.
SOURCE: Adv. Exp. Med. Biol. (1989), 257(Immune Response Viral Infect.), 187-92
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 8 refs. on the construction of recombinant R7020, the problem of evaluating biol. properties of prototype herpes simplex virus vaccines, attenuation of R7020, R7020 as an immunogen, and genetic stability of R7020.

L3 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:513330 HCAPLUS
DOCUMENT NUMBER: 113:113330
TITLE: Isolated gA/gB glycoprotein complex of human cytomegalovirus envelope induces humoral and cellular immune-responses in human volunteers
AUTHOR(S): Gonczol, Eva; Ianacone, John; Ho, Wenzhe; Starr, Stuart; Meignier, Bernard; Plotkin, Stanley
CORPORATE SOURCE: Wistar Inst. Anat. Biol., Philadelphia, PA, USA
SOURCE: Vaccine (1990), 8(2), 130-6
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three human cytomegalovirus (HCMV) seroneg. individuals were immunized with a single dose of HCMV envelope; 2 individuals developed neutralizing antibodies. Naturally HCMV seropos. and HCMV seroneg. human volunteers were immunized with a major glycoprotein complex, gA/gB, of HCMV that had been purified by immunoabsorbent column chromatog. After a single injection of the gA/gB prepn., the naturally seropos. individuals developed higher titers of neutralizing antibodies and temporarily higher HCMV-specific lymphocyte proliferation (HCMV-LP) response in vitro. The seroneg. individuals developed neutralizing antibodies after the third injection of gA/gB, which were present only transiently, but showed a rapid reappearance and increase in titer after the fourth injection. At 1 yr after the first injection, the neutralizing antibody titers were still comparable with those of the naturally seropos. individuals. HCMV-LP responses to HCMV in the initially seroneg. individuals developed after the second or third injection with the gA/gB prepn. and remained pos. during the 1-yr observation period. Thus, the gA/gB protein induces both humoral and cellular immune responses in humans, and might serve as the

basis of a subunit vaccine.

L3 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:471936 HCAPLUS
DOCUMENT NUMBER: 111:71936
TITLE: Genetic engineering of novel herpes simplex virus (HSV) genomes for use as potential vaccines and as vectors of foreign genes
AUTHOR(S): Meignier, B.; Roizman, B.
CORPORATE SOURCE: Inst. Merieux, Marcy-l'Etoile, Charbonnieres-les-Bains, 69752, Fr.
SOURCE: Int. Biotechnol. Symp., 8th (1988), Volume 2, 740-5.
Editor(s): Durand, G.; Bobichon, L.; Florent, J. Soc. Fran. Microbiol.: Paris, Fr.
CODEN: 560AA7
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 8 refs., on the construction of a live attenuated herpes simplex virus vaccine. Discussion includes cloning strategy; evaluation of biol. properties, attenuation; immunogenicity and genetic stability of the recombinant virus.

L3 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:52021 HCAPLUS
DOCUMENT NUMBER: 110:52021
TITLE: In vivo behavior of genetically engineered herpes simplex viruses R7017 and R7020: construction and evaluation in rodents
AUTHOR(S): Meignier, Bernard; Longnecker, Richard; Roizman, Bernard
CORPORATE SOURCE: Inst. Merieux, Marcy l'Etoile, Fr.
SOURCE: J. Infect. Dis. (1988), 158(3), 602-14
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The herpes simplex virus (HSV) recombinant R7017 was constructed from HSV-1 (strain F) by deleting a portion of the thymidine kinase (tk) gene and by replacing the sequences representing the internal inverted repeats and adjacent genes in the L component with a fragment of the HSV-2 genome encoding the glycoproteins G, D, I, and a portion of E. In addn., the R7020 recombinant contains an HSV-1 DNA fragment encoding the tk gene fused to the .alpha.4 gene promoter. The results of studies in mice, guinea pigs, and rabbits were as follows: Both recombinants remained unchanged after 9 serial, intracerebral passages in mice; the recombinants could not be differentiated with respect to attenuation in mice injected intracerebrally, in vaginally infected guinea pigs, and in rabbits inoculated on the scarified cornea. Given intradermally or i.m., the recombinants prevented severe infections by virulent challenge viruses, and R7020 established latent infections (at a low frequency) in all species tested, whereas latent R7017 virus was detected in rabbits only.

L3 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:109390 HCAPLUS
DOCUMENT NUMBER: 108:109390

TITLE: Virulence of and establishment of latency by genetically engineered deletion mutants of herpes simplex virus I

AUTHOR(S): Meignier, Bernard; Longnecker, Richard; Mavromara-Nazos, Penelope; Sears, Amy E.; Roizman, Bernard

CORPORATE SOURCE: Inst. Merieux, Charbonnieres les Bains, 69752, Fr.

SOURCE: Virology (1988), 162(1), 251-4

CODEN: VIRLAX; ISSN: 0042-6822

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The biol. properties of 7 deletion mutants of herpes simplex virus 1 (HSV-1) were exmd. The genes deleted from 6 of these mutants map in the S component of HSV-1 DNA and include those specifying the .alpha. protein 47, the glycoproteins G and E, the viral protein kinase, and 2 proteins whose functions are not yet known (open reading frames US2 and US11). The 7th virus [HSV-1(F).DELTA.305] contained a 700-bp deletion in the thymidine kinase gene. The results of intracerebral inoculation of Balb/c mice indicated that all but one of the deletion mutants in the S component were significantly attenuated. The PFU/LD50 ratios for these mutants ranged from 104- to 105-fold higher than that of the wild-type, HSV-1(F). The PFU/LD50 for mutant R7032, from which the glycoprotein E gene was deleted, was <100-fold higher than that of the parent virus. All of the mutants, with 1 exception, were able to establish latency in mice; the exception, HSV-1(F).DELTA.305, was able to establish latency in rabbits.

L3 ANSWER 23 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:30791 HCPLUS

DOCUMENT NUMBER: 106:30791

TITLE: Analyses of transplanted murine tumors for HSV DNA sequences

AUTHOR(S): Yehiely, Fruma; Thuning, Claire; Meignier, Bernard; Norrild, Bodil; Warren, Joel; Nahmias, Andre J.; Rapp, Fred; Roizman, Bernard; Frenkel, Niza Kovler Viral Oncol. Lab., Univ. Chicago, Chicago, IL, USA

CORPORATE SOURCE: Int. J. Cancer (1986), 38(3), 395-403

SOURCE: CODEN: IJCNAW; ISSN: 0020-7136

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In a companion paper, the results of exposure of C57BL/6NCr mice to vaginal plugs contg. live or inactivated herpes simplex virus 1 or 2 (HSV-1 or HSV-2) or recombinant viruses 5 times a week for up to 114 wk are reported. Genital organs showing abnormalities were transplanted into nude mice. Of 33 transplants, 13 produced s.c. tumors in nude mice and 12 were subsequently transplanted into C57BL/6NCr mice. In this study, the DNA extd. from coded tumor tissues of nude mice and from normal viscera of the same rodents did not hybridize with HSV-1 and HSV-2 DNA probes representing the viral genomic regions shown previously to be capable of morphol. transforming cells in culture. The sensitivity of the assays was such that 0.5 copies of the HSV sequences of complexity equal to or greater than 1 Kbp per cell DNA equiv. could be detected. To control for the sensitivity of the assays in the actual hybridizations, the tumor-cell DNA was also hybridized with a .beta.-globin mouse DNA probe. A striking

feature of these control hybridizations was the detection of .beta.-globin polymorphism in some nude mouse tumors. Thus, the analyzed tissues contained significant amts. of the tumor cells occurring in the C57BL/6NCr mice.

L3 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:180753 HCAPLUS
DOCUMENT NUMBER: 104:180753
TITLE: Genetically engineered genomes of herpes simplex virus 1: structure and biological properties
AUTHOR(S): Roizman, Bernard; Sears, Amy E.; **Meignier, Bernard**; Arsenakis, Minas
CORPORATE SOURCE: Marjorie B. Kovler Viral Oncol. Lab., Univ. Chicago, Chicago, IL, 60637, USA
SOURCE: Banbury Rep. (1985), 22(Genet. Altered Viruses Environ.), 251-63
DOCUMENT TYPE: CODEN: BANRDU; ISSN: 0198-0068
Journal; General Review
LANGUAGE: English
AB A review with 22 refs. on the capacity of genetically engineered strains of herpes simplex virus 1, carrying specific insertions or deletions, to establish latency and cause disease.

L3 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:555005 HCAPLUS
DOCUMENT NUMBER: 103:155005
TITLE: Herpes simplex virus 1 mutant deleted in the .alpha.22 gene: growth and gene expression in permissive and restrictive cells and establishment of latency in mice
AUTHOR(S): Sears, Amy E.; Halliburton, Ian W.; **Meignier, Bernard**; Silver, Sandra; Roizman, Bernard
CORPORATE SOURCE: Marjorie B. Kovler Viral Oncol. Lab., Univ. Chicago, Chicago, IL, 60637, USA
SOURCE: J. Virol. (1985), 55(2), 338-46
DOCUMENT TYPE: CODEN: JOVIAM; ISSN: 0022-538X
Journal
LANGUAGE: English
AB R325-.beta.TK+ a herpes simplex virus 1 mutant carrying a 500-base-pair deletion in the .alpha.22 gene and the wild-type (.beta.)thymidine kinase (TK) gene, was previously shown to grow efficiently in HEp-2 and Vero cell lines. In rodent cell lines, exemplified by the Rat-1 line, plating efficiency was reduced and growth was multiplicity dependent. A similar multiplicity dependence for growth and lack of virus spread at low multiplicity was seen in resting, confluent human embryonic lung (HEL) cells. The shutoff of synthesis of .beta. proteins was delayed and the duration of synthesis of .gamma. proteins was extended in R325-.beta.TK+-infected HEL cells relative to cells infected with the wild-type parent, but no significant differences were seen in the total accumulation of viral DNA. To quantify the effect on late (.gamma.2) gene expression, a recombinant carrying the deletion in the .alpha.22 gene and a .gamma.2-TK gene (R325-.gamma.2TK) was constructed and compared with a wild-type virus (R3112) carrying a chimeric .gamma.2-TK gene. In Vero cells, the .gamma.2-TK gene of R325-.gamma.2TK was expressed earlier than and at the same level as the .gamma.2-TK gene of R3112. In the confluent

resting HEL cells, the expression of the .gamma.2-TK gene of the .alpha.22- virus was grossly reduced relative to that of the .alpha.22+ virus. Electron microscopic studies indicated that the no. of intranuclear capsids of R325-.beta.TK+ virus was reduced relative to that of the parent virus in resting confluent HEL cells, but the no. of DNA-contg. capsids was higher. Notwithstanding the grossly reduced neurovirulence on intracerebral inoculation in mice, R325-.beta.TK+ virus was able to establish latency in mice. Thus, the .alpha.22 gene affects late (.gamma.2) gene expression, and a host cell factor complements that function of the .alpha.22 gene to a greater extent in HEp-2 and Vero cells than in confluent, resting HEL cells.

L3 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1985:538331 HCAPLUS

DOCUMENT NUMBER: 103:138331

TITLE: Establishment of latency in mice by herpes simplex virus 1 recombinants that carry insertions affecting regulation of the thymidine kinase gene

AUTHOR(S): Sears, Amy E.; Meignier, Bernard; Roizman, Bernard

CORPORATE SOURCE: Marjorie B. Kovler Viral Oncol. Lab., Univ. Chicago, Chicago, IL, 60637, USA

SOURCE: J. Virol. (1985), 55(2), 410-16
CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Herpes simplex virus I recombinants carrying .alpha.-, .beta.-, and late .gamma. (.gamma.2)-regulated thymidine kinase (TK) genes were tested for the ability to establish latency in BALB/c mice inoculated by the eye route. Representatives of .alpha.- and .gamma.2-regulated TK recombinants all established and maintained latent infections, but the efficiency was lower than that of wild-type virus. Of the 3 .alpha.TK recombinants tested, one (R316) spontaneously deleted portions of the inserted sequences which conferred .alpha. regulation to the TK gene. The viruses carrying these deletions expressed considerably lower TK activity than did wild-type virus, i.e., 2-40% of the levels expressed by the wild-type virus carrying the .beta.TK gene. However, the ability of these viruses to establish latency was not related to the efficiency of expression of the TK gene. Thus, the conversion of the TK gene into an .alpha. or .gamma.2 gene did not preclude the establishment of latent infections. There was no correlation between the levels of of TK activity expressed in cell culture and the ability to establish latency. Rearrangement of the genome by insertions or deletions which interrupt gene domains did not automatically result in an inability to establish latent infections.

L3 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:173945 HCAPLUS

DOCUMENT NUMBER: 98:173945

TITLE: Application of molecular genetics to the design of live herpes simplex virus vaccines

AUTHOR(S): Roizman, Bernard; Warren, Joel; Thuning, Claire Ann; Fanshaw, Miriam S.; Norrild, Bodil; Meignier, Bernard

CORPORATE SOURCE: Marjorie B. Kovler Viral Oncol. Lab., Univ. Chicago,

Hines 09/746,581 < page>

SOURCE: Chicago, IL, 60637, USA
Dev. Biol. Stand. (1982), 52(Herpes Virus Man Anim.:
Stand. Immunol. Proced.), 287-304
CODEN: DVBSA3; ISSN: 0301-5149
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 30 refs.

L3 ANSWER 28 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:153854 HCPLUS
DOCUMENT NUMBER: 94:153854
TITLE: Culturing of animal cells on microsupports
AUTHOR(S): Meignier, B.; Merieux, Iffa
CORPORATE SOURCE: Lyon, 69007, Fr.
SOURCE: Cell. Immobilisees, Colloq. (1979), 45-70. Soc. Fr.
Microbiol.: Paris, Fr.
CODEN: 45EQAL
DOCUMENT TYPE: Conference; General Review
LANGUAGE: French
AB A review with 40 refs. on the culturing of animal cells on microsupports
and their use in the pharmaceutical industry.